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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/641,742

08/18/2000

Samuel J. Danishefsky

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SLOAN-KETTERING INSTITUTE FOR CANCER RESEARCH
TWO INTERNATIONAL PLACE
BOSTON, MA 02110

EXAMINER

CANELLA, KAREN A

ART UNIT

PAPER NUMBER

1643

MAIL DATE

DELIVERY MODE

04/17/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

09/641,742

Applicant(s)

DANISHEFSKY ET AL.

Examiner

Karen A. Canella

Art Unit

1643

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 56, 58-62, 65-67, 69-76, 78-81, 84-86 and 88-102 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 56, 58-60, 62, 65-67, 69-76, 78-81, 84-86 and 88-102 is/are rejected.
- 7) ☒ Claim(s) 61 is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date ____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date ____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: ____

DETAILED ACTION

After review and reconsideration, the finality of the Office action of January 7, 2009 is withdrawn.

The amendment filed March 19, 2009 has been entered. Claim 55, 72, 74, 76, 93 and 96 have been amended. Claims 56, 58-62, 65-67, 69-76, 78-81, 84-86, 88-102 are pending and under consideration.

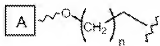
The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 62, 65, 66, 70, 71, 74, 75, 81, 84, 85, 88, 89, 90, 92, 93, 94, 99 and 101 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

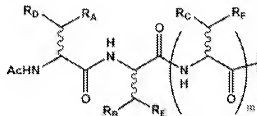
It is unclear how the structure recited in claims 62, 74, 81, 99 can further modify claims 56, 62, 76, 72 requiring the alkyl glycosidic moiety..

Further, it is unclear how the alkyl glycosidic moiety



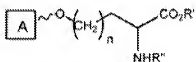
accommodates the structure

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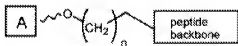


in claims 85 and 101.

The specification teaches (page 6) that the alkyl glycosidic moiety is attached to the backbone of an amino acid:



or the backbone of a peptide:



Therefore the alkyl glycosidic moiety having only methylene groups as depicted in the claims cannot accommodate R_A , R_B or R_C being methyl when attached at the amino acid backbone as indicated. Thus the scope of claims 85 and 101 characterized by both the glycosidic moiety and the polypeptide structure wherein R_A , R_B or R_C being methyl is unclear and it is unclear how claims 62, 74, 81, 99 can further modify claims 56, 62, 76, 72 for the same reasons.

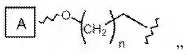
The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

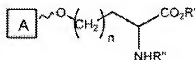
pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 56, 58-60, 67, 69, 72, 73, 76, 78-80, 86, 91, 92, 95-98, 100 and 102 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

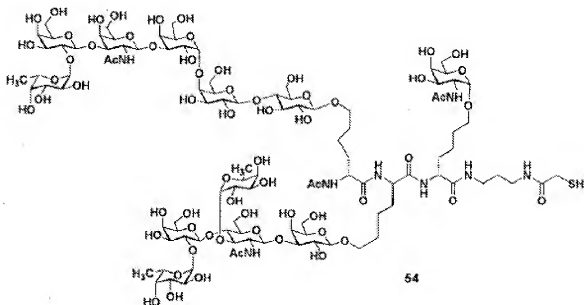
Claims 56, 72, 73, 76, 91 and 96 recite "glycopeptide comprising a peptide backbone made up of at least three amino acid residues, wherein two or more of said amino acids are independently substituted with a glycosidic moiety having the structure:



When given the broadest reasonable interpretation, "substituted with a glycosidic moiety" of the above structure does not limit the claims to substitution directly on the "peptidic backbone", as amino acid side chains can be substituted, nor does it limit the claims to substitution on the alpha carbon but include substitution of the peptide backbone on nitrogen of the peptide linkage and the carbonyl carbon, all of which are considered to be part of the peptide backbone.. The specification teaches structures in which the "glycosidic moiety" is linked directly to an amino acid at the alpha carbon

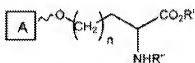


and peptides comprising such amino acids:



However, these examples fail to adequately describe a genus of molecules characterized by a peptide comprising three of amino acids substituted with the glycosidic moiety, because the location of the substitution is undefined and can occur anywhere along the peptide chain, including the carbonyl or amino group, side chains or termini. One of skill in the art would reasonably conclude that applicant was not in possession of the entirety of the invention at the time of filing.

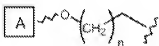
Claims 56, 58-60, 67, 69, 72, 73, 76, 78-80, 86, 91, 92, 95-98, 100 and 102 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for multi-antigenic glycopeptides formed from carbohydrate determinants selected from the group consisting of Globo-H, fucosyl GM1, KH-1, glycophorin, sTN, Le-Y, N3, Tn, 2,6-sTN, (2-3)-ST, TF, wherein the peptide is formed from amino acids having a glycosidic moiety attached to the alpha carbon, as in



does not reasonably provide enablement for multi-antigenic glycopeptides formed from carbohydrate determinants selected from the group consisting of Globo-H, fucosyl GM1, KH-1, glycophorin, sTN, Le-Y, N3, Tn, 2,6-sTN, (2-3)-ST, TF wherein the carbohydrate domains are attached to the peptide at locations other than the alpha carbon of a glycine amino acid within the peptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re wands, 858 F.2d 731, 737.8 USPQ2d 1400, 1404 (Fed. Cir. 1988)..

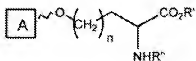
Claims 56, 72, 73, 76, 91 and 96 recite "glycopeptide comprising a peptide backbone made up of at least three amino acid residues, wherein two or more of said amino acids are independently substituted with a glycosidic moiety having the structure:



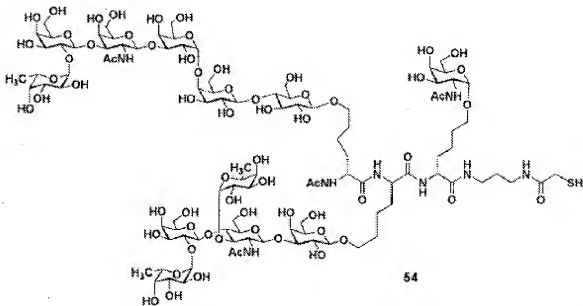
When given the broadest reasonable interpretation, "substituted with a glycosidic moiety" of the above structure does not limit the claims to substitution directly on the "peptidic backbone", as amino acid side chains can be substituted, nor does it limit the claims to substitution on the alpha carbon but include substitution of the peptide backbone on nitrogen of the peptide linkage and the carbonyl carbon, all of which are considered to be part of the peptide

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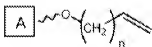
backbone.. The specification teaches how to make structures in which the "glycosidic moiety" is linked directly to an amino acid at the alpha carbon



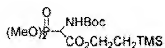
and peptides comprising such amino acids:



The specification teaches that the coupling of the carbohydrate domain provided as an allyl glycoside having the structure



which is subjected to ozonolysis to the aldehyde, followed by and Horner-Emmons olefination using a phosphonate

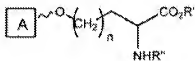


to transfer the synthon of an amino ester, followed by asymmetric hydrogenation and deprotection to produce the glycoamino acid.

First, it appears that only a modified glycine can be formed using this synthetic method because the phosphonate requires loss of a proton on the alpha carbon as indicated in J. March, (Advanced Organic Chemistry, 2nd edition, 1977, page 867, top of the page). Second it appears that the only attachment point of the glycosidic moiety is through coupling with the alpha carbon of the amino acid. Thus, the specification fails to teach how to make the multi-antigenic peptides wherein the glycosidic moiety is attached to any other atom in the peptide. One of skill in the art would be forced into undue experimentation in order to make the broadly claimed multi-antigenic glycoproteins of the invention because the art of organic synthesis is unreliable with respect to highly functionalized molecules, which are the molecules encompassed by the claims.

The art teaches that organic synthesis of a multifunctional molecule is not trivial undertaking. The art teaches that presence of differing functional groups, heteroatoms and three dimensional configurations require different considerations as to protecting groups, and reactivity manifest in different synthetic strategies (Sierra and de la Torre, *Angewandte Chemie*, 2000, Vol. 39, pp. 1538-1559, especially pages 1544-1546, "Troublesome Protecting Groups", cited in the Office action of July 13, 2007). Chemical structure heterogeneity including the presence of different heteroatoms on different three dimensional structures can radically alter the reactivity of any other atom within a molecule through inductive effects (page 1545, second column, lines 2-6 of the second full paragraph and lines 4-7 of the third full paragraph, resonance effects, acidity, basicity and steric hindrance (page 1552-1554), strain (page 1554-1557) or transition state crowding (page 1545, second column, second full paragraph, lines 2-6., page 1546, second column, first full paragraph) and therefore can radically influence the reactivity

with any given reagent contacted thereto. Sierra and de la Torre teach that a well-testing transformation can fail for complex reasons (Sierra and de la Torre, *ibid*, page 1540, first column, lines 9-11, page 1541, first column, lines 33-37, under the heading "Working Models that do not Work", page 1542, first column, lines 15-17, even when supported by molecular mechanics calculations (page 1542, first column, lines 6-9) and what is seen as an innocuous alteration can cause a failure in a synthetic step (page 1542, second column, lines 9-12). Sierra and de la Torre teach that the presence of remote substitutions has unexpected influence over a chemical step (pages 1546-1548, under the heading "The Unexpected Influence of Remote Substituents") Sierra and de la Torre state that "As the complexity of intermediates increases, the number of variables involved in a simple transformation grow exponentially making predictions about the outcome of any given synthetic step on a highly functionalized intermediate, unreliable (page 1548, second column, lines 5-8 of the second full paragraph, page 1550, second column, lines 1-9 under the heading "The Trivial Functional Group Transformation"). Sierra and de la Torre conclude that the lack of predictability in so many cases and the very empirical nature of synthetic organic chemistry implies that the science is not fully developed (page 1548, second column, lines 13-16 of the second full paragraph). Sierra and de la Torre state that alternate routes can then be devised which circumvent a failed transformation (page 1548, second column, lines 10-13 of the second full paragraph), however, the sum total effort of designing and redesigning represents undue experimentation to one of skill in the art, exemplified by Sierra and de la Torre as "the amount of effort devoted to simple transformations is still quite enormous" (page 1557, first column, lines 15-18). The specification provides no means of making said compounds which have linkages to amino acids in a peptide beyond that of



.Thus, one of skill in the art would be subject to undue experimentation in order to make and use the broadly claimed compounds encompassed by the claims.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 62, 65, 70, 71, 74, 75, 81, 84, 85, 88-90, 92-94, 99 and 101 are rejected under 35 U.S.C. 102(e) as being anticipated by Danishefsky et al (U.S. 6,660,714).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention “by another,” or by an appropriate showing under 37 CFR 1.131.

Danishefsky et al discloses the instant glycoconjugates having a peptide backbone made up of at least three amino acids, wherein each occurrence of RD, RE and RF is independently a carbohydrate domain that includes the instant polysaccharides (see claim 6 of '714, for example) Danishefsky et al disclose carriers of BSA, polylysine, KLH, tripalmitoyl-S-glycerylcysteinylserine and compositions comprising bacterial adjuvants such as BCG, Salmonella minnesota and QS21 which is a saponin (see claims 51, 52, 56 and 57). The disclosure of glycopeptides comprising independent carbohydrate domains encompasses glycopeptides having different carbohydrate domains for RD, RE and RF, which is commensurate with having multiple carbohydrate domains. Danishefsky et al teach the cross linker of claim 65 (see columns 17-18). Thus the disclosure of the '714 patent encompasses constructs which comprises independent carbohydrate domains that are not identical and thus anticipates the instant claims for a multi-antigenic construct..

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 62, 65, 70, 71, 74, 75, 81, 84, 85, 88-90, 92-94, 99 and 101 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-47 of U.S. Patent No. 7,160,856. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '856 patent anticipate the instant claims. It is noted that claims of the patent include multi-antigenic constructs because the carbohydrate domains are independently selected from Tn, sTn, sT, etc (see claim 3 of '856).

Applicant argues that the patent discloses structures that are carbohydrate domain attached to natural amino acids such as serine and threonine and not the claimed subject matter of the instant claims which requires a synthetic linkage between the carbohydrate domains and

the peptide backbone. This has been considered but not found persuasive. It is noted that the '856 patent discloses the same structural features of the instant claims: for example, claim 4 of the '856 patent versus the instant claim 62. Applicant argues below that the instant claims require at least two carbon atoms between the carbohydrate domain and the peptide backbone by virtue of the limitation in claim 56, wherein $n=1-8$, however this limitation does not exclude the subject matter of the '714 patent. It is noted that the structure of claim 1 of the '856 patent and the structure of the instant claim 62 both utilize a "squiggly" line to indicate attachment of the carbon bearing the carbohydrate domain to the peptide backbone. One of skill in the art would obviously know that the squiggly line is not limited to a single carbon-carbon bond, but is used to indicate some form of attachment. The specification can be used as a dictionary to learn the meaning of a term in the patent claim. *Toro Co. v. White Consol. Indus., Inc.*, 199 F.3d 1295, 1299, 53 USPQ2d 1065, 1067 (Fed. Cir. 1999). Thus, Figure 1 of the '856 patent indicates that link between the carbohydrate domain and an alpha serine carbon facilitate the attachment of the carbohydrate domain to the peptide backbone. One of skill in the art would reasonable conclude that the "squiggly" encompasses a linkage between the carbohydrate domain and the peptide backbone of two carbons. This linkage fulfills the specific requirement of the instant claim 56 for $n=1$, and a linkage of two methylene groups. It is further noted that there are no claim limitations in the instant case which would prohibit the use of a peptide comprising all serines so as to accommodate the $n=1$ limitation in claim 56. Thus applicant's arguments that the '856 patent does not encompass structures of the instant invention are unpersuasive.

Claims 62, 65, 66, 70, 71, 74, 75, 81, 84, 85, 88-90, 92-94, 99, and 101 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-58 of U.S. Patent No. 6,660,714. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are drawn to the products and compositions used in the method claims of the '714 patent. Thus the instant claims are obvious over the method claims of the patent.

Applicant argues that the claims of the '714 patent are methods of using the glycopeptides of U.S. 7,160,856. This has been considered but not found persuasive. The

claims of the '714 patent, although drawn to methods, disclose the same structures as the claims in the '856 patent, and therefore anticipate the instant claims for the same reasons of record as that of the '856 patent.

Applicant argues that both of the '714 and '856 patents are limited by "one carbon atom" between the glycosidic moiety and the peptide backbone which is in contrast to the instant claims which requires "two carbon atoms" between the carbohydrate domain and the peptide backbone. This has been considered but found only partially persuasive. Because of the vague and indefinite nature of the rejected claims in terms of the structure of the glycosidic moiety as attached to the peptide backbone, the claims remain rejected.

Applicant argues that a Declaration has been previous submitted under 37 CFR 1.132 to aver that the invention described in the '714 patent was derived from the inventors or the instant application and therefore not invented "by another". This has been considered but not found persuasive for the reasons of record cited on page 3 the Office action of July 25, 2008, namely, the invention under rejection in the '714 patent is claimed [emphasis added] (claims 6, 51, 52 and 56) rather than disclosed but not claimed. Therefore the Declaration fails to overcome the outstanding rejection.

Claims 62, 66, 71, 81, 85, 88, 90, 92, 99 and 101 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 87, 88, 108, 109, 129, 130, 134, 135, 155-161 of copending Application No. 10/898,410. Although the conflicting claims are not identical, they are not patentably distinct from each other because the structures of the '410 application anticipate the instant claims to the extent that PamCys, (palmitoyl-S-glycerylcysteinyserine) which is part of the structure, functions as a carrier.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

All other rejections and objections as set forth or maintained in a prior Office action are withdrawn.

Claim 61 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Karen A Canella/
Primary Examiner, Art Unit 1643